REMARKS

I. Amendments to the Claims

Applicants have made minor amendments to the claims to improve clarity and consistency in the terminology used. For example, claims 1, 3, 6, 8, 11, 12, and 21 have been amended to recite "at least one drug"; claims 1, 2, 3, and 16 have been amended to delete the functional language "that improves resilience of the microgranules"; claim 4 has been amended to refer to "taste-masked microgranules"; and claim 21 has been amended to delete redundant language. These amendments are supported by the claims as originally filed.

Applicants submit that these amendments would not introduce new issues requiring further search or examination. No new matter is believed to have been added. Claims 1-24 are active.

II. Rejection under 35 U.S.C. § 102(b)

The rejection of claims 1-24 under 35 U.S.C. § 102(b) over *Ohta* (EP 0 914 818 A1) is respectfully traversed. The Examiner states that *Ohta* "meets the structural limitations of the instant claims" even though *Ohta* "does not explicitly teach about a taste-masked microcapsule (the intended use)". Applicants respectfully disagree for the reasons indicated below.

The tablets of the claimed invention comprise, in part, taste-masked microcapsules. As stated in claim 1, taste-masked microcapsules are prepared by first granulating "at least one drug ... and at least one polymeric binder", "wet milling" the resulting "granulated mass", then "microencapsulating the milled granules" (emphasis added). As discussed in the present specification, an exemplary method for microencapsulating granules containing the "active" (*e.g.*, drug) is coacervation, in which drug-containing particles are dispersed in a microencapsulation solution, *e.g.*, containing a taste-masking polymer such as ethylcellulose. Upon cooling the microencapsulation solution, the taste-masking polymer is then deposited as a film or membrane over the drug-containing polymer.[1] Thus, while not limited to a specific microencapsulation process or microencapsulation composition, the microencapsulation step of the claimed invention clearly requires that the "milled granules"

[1] *E.g.*, present specification at ¶ [0029]

comprising at least one drug and at least one polymeric binder are coated (*i.e.* microencapsulated) with a microencapsulating layer, *e.g.* ethylcellulose as exemplified in Examples 2-7. Thus, even if the term "taste-masked" is deemed an "intended use", the "microencapsulating" step reasonably requires a structural feature (*i.e.*, a microencapsulation coating on the drug-containing microcapsule) not found in *Ohta*. Thus, the structure of the taste-masked microcapsules of the claimed tablet is different from that of the drug-containing particles of *Ohta*.

In addition, claim 1 specifies that the claimed tablets comprise a "compressed blend" of two types of particles, (1) "rapidly dispersing microgranules" and (2) "taste-masked microcapsules". The composition and structure of the taste-masked microcapsules are discussed above. The rapidly dispersing microgranules are prepared by granulating 30 μm or less particles of a sugar alcohol and/or a saccharide, and a disintegrant. These two types of particles (*i.e.*, rapidly dispersing microgranules and taste-masked microcapsules) are then mixed and compressed to form tablets having discrete rapidly dispersing microgranules and taste-masked microcapsules therein.

In distinct contrast, *Ohta* only describes tablets prepared by granulating a single mixture comprising a sugar alcohol or saccharide, an "active ingredient", a disintegrant, and optionally a binder or other excipients. This process would reasonably provide a single type of particle containing a combination of all of these ingredients, which is then compressed into a tablet.[2]

Thus, the tablets of the present invention and those of *Ohta* differ significantly in that the claimed tablets comprise two types of particles whereas those of *Ohta* comprise only a single type of particle, and *Ohta* does not describe taste-masked microcapsules having a microencapsulation coating as in the claimed tablet.

Moreover, since the tablets of the claimed invention and those of *Ohta* have significantly different structures, the dissolution profile of the tablets of *Ohta* cannot reasonably be inherently (*i.e.* necessarily) like those of the claimed tablets.

Accordingly, *Ohta* cannot reasonably anticipate the claimed invention. Applicants respectfully request that the rejection be withdrawn.

---

[2] *Ohta*. ¶¶ [0018]-[0023]

III. Rejection under 35 U.S.C. § 103(a)

The rejection of claims 1, 11, and 12 under 35 U.S.C. §103(a) over the combination of *Ohta* and *Cherukuri* (US 2002/0044962), and the rejection of claims 1-24 over the combination of *Percel* (US 6451345) and *Masaki* (US 5466464) are respectfully traversed.

A. *Ohta* and *Cherukuri*

The Examiner argues that "*Ohta* meets the claim limitations ... but fails to include [a] pharmaceutically active agent such as sumatriptan." Applicants respectfully disagree with this analysis for the following reasons.

First, for the reasons stated above in section II of this Response, *Ohta* does not meet the limitations of claim 1 (and therefore claims 11 and 12 which ultimately depend from claim 1) because *Ohta* does not describe taste-masked microcapsules having a microencapsulation coating, and the tablets of *Ohta* comprise a single type of granule, whereas the tablets of the claimed invention comprise two types of particles (*i.e.*, rapidly disintegrating granules and taste-masked microgranules).

Moreover, *Cherukuri* does not remedy the deficiencies of *Ohta*. *Cherukuri* describes caplets[3] comprising a single type of granule prepared by granulating together the active ingredient and erodible polymer together in the presence of a binder[4], lubricating the resulting granules with a lubricant and compressing them to form a caplet.[5] After compression, the finished caplet may be coated with *e.g.* an extended release coating[6] and loaded into capsules.[7] In another embodiment, *Cherukuri* also describes tablets "with swelling polymers, osmotic ingredients and [an] active substance", wherein the entire tablet is coated with a "film-forming polymer". Thus, the encapsulated caplets or tablets of *Cherukuri* are coated after compressing the constituent granules, whereas in the claimed tablets, the constituent drug-containing microgranules are coated (microencapsulated) for taste-masking before compression into the final tablet form. As a result, the structures of the claimed tablets and

[3] *Cherukuri*, ¶ [0041]
[4] *Ibid.*, ¶¶ [0052]-[0055]
[5] *Ibid.*, ¶ [0057]
[6] *Ibid.*, ¶¶ [0060]-[0062]
[7] *Ibid.*, ¶ [0161]

those of *Cherukuri* are quite different. Accordingly, *Cherukuri* does not describe tablets comprising taste-masked microcapsules, as in the claimed invention.

Since neither *Ohta* nor *Cherukuri* teach tablets comprising microencapsulated drug-containing granules, their combination must also lack this limitation of the claimed invention. Accordingly, Applicants respectfully submit that the combination of *Ohta* and *Cherukuri* fails to support a *prima facie* case of obviousness.

In addition, Applicants note that neither *Ohta* nor *Cherukuri* describe the average particle size of the microencapsulated taste-masked microcapsules (*i.e.*, claims 2, 16) or the average particle size of the drug (*i.e.*, claims 3, 4, 6, 21, and 24). Accordingly, Applicants respectfully submit that the combination of *Ohta* and *Cherukuri* also fails to support a *prima facie* case of obviousness for these dependent claims.

Furthermore, Applicants note that the tablets of *Ohta* are orally disintegrating[8] and inherently have immediate release properties (*i.e.*, because the drug-containing granules are uncoated). *Cherukuri*, in contrast, describes tablets or caplets which the skilled artisan would recognize as having substantially different properties compared to those of *Ohta*. The tablets or caplets of *Cherukuri* are disintegrant-free and are filled into capsules. Thus, they are intended to be swallowed *whole* for absorption in the lower GI tract, since capsules containing a disintegrant-free composition would not reasonably be expected to disintegrate in the oral cavity. In addition, the tablets or caplets of *Cherukuri* are clearly not intended as immediate release formulations because they are coated with a controlled or extended release coatings (which are designed to impede release of the drug).

Because the compositions of *Ohta* and *Cherukuri* are so different, there is no reasonable suggestion or motivation to combine their teachings because doing so would reasonably render the dosage forms of either reference unsuitable for their intended use, and/or change their respective principles of operation (*see* MPEP 2143.01 (V) & (VI)). For example, modifying the orally disintegrating tablets of *Ohta* to include the controlled or extended release coating of *Cherukuri* (*i.e.*, to the exterior of the entire tablet as taught by *Cherukuri*) would reasonably provide a tablet with extended release properties, rather than the immediate release properties of the tablets of *Ohta*. Alternatively, modifying the

[8] *Ohta*, ¶ [0003]

compositions of *Cherukuri* to include the disintegrant-containing granules of *Ohta* would reasonably provide caplets or tablets which no longer have controlled or extended release properties. Accordingly, as a matter of well-settled law, there is no reasonable motivation or suggestion to combine *Ohta* and *Cherukuri*. Applicants therefore request that the rejection be withdrawn.

B. *Percel* and *Masaki*

The Examiner states that the "*Percel* reference in combination with *Masaki['s]* teaching provides [the] desired dissolution and taste-masking formulations in the form [of] tablets along with similar binders and other comment excipients." The Examiner's arguments appear to focus on the dissolution profile limitation of the pending claims, but do not specifically address how the combined teachings of *Percel* and *Masaki* provide the composition and structure of the claimed tablets. Applicants respectfully submit that the compositions and structures of the tablets of both *Percel* and *Masaki* are substantially different from the claimed tablets, and their combination does not teach all of the limitations of the claimed invention.

Percel describes taste-masked granules of linezolid in which the linezolid is microencapsulated (*e.g.* by coacervation), then coated with an optional seal coating and an enteric coating.[9] These granules may be incorporated into a "fast disintegrating tablet formulation" in which the taste-masked linezolid granules are blended with various ingredients and compressed into tablets.[10] However, the taste-masked granules of linezolid of *Percel* are quite different from the taste-masked microcapsules claimed invention. The taste-masked microcapsules of the claimed invention comprise a combination of a drug and "at least one polymeric binder" which is subsequently microencapsulated. In contrast, the linezolid granules of *Percel* are prepared by microencapsulating linezolid "crystals"[11], and thus do not contain a binder. Thus, *Percel* does not teach the taste-masked microgranules of the claimed invention.

[9] *Percel*, col. 1, lines 47-53
[10] *Ibid.*, Examples 5-7
[11] *Ibid.*, Example 1

In addition, the "fast disintegrating" tablets of *Percel* are prepared by simply combining the microencapsulated linezolid crystals with additional ingredients and compressing the resulting mixture to form a tablet, rather than separately combining a sugar alcohol or saccharide and a disintegrant into a discrete, rapidly dispersing microgranule. Thus, the tablets of *Percel* also do not include the rapidly dispersing microgranules of the claimed invention. Furthermore, *Percel* is silent in regard to the particle size of the sugar alcohol.

Thus, *Percel* does not describe a tablet comprising two different types of particles, taste-masked microgranules, rapidly dispersing microgranules, or the particle size of the sugar alcohol.

Masaki does not remedy these deficiencies of *Percel*. *Masaki* describes "intrabuccally disintegrating" compositions comprising the combination of a sugar alcohol, agar, and an active ingredient. These compositions are prepared by suspending the active ingredient, sugar alcohol, optionally other excipients, in an aqueous agar solution, filling the suspension into a mold, and then drying.[12] Thus, the tablets of *Masaki* do not include taste-masked particles comprising a microencapsulated drug/binder, rapidly dispersing microgranules comprising a sugar alcohol and disintegrant, or tablets comprising a compressed blend of taste-masked microcapsules and rapidly dispersing microgranules.

Since neither *Percel* nor *Masaki* describe the taste-masked microcapsules or rapidly dispersing microgranules of the present invention, and both are silent in regard to the particle size of the sugar alcohol, the combination of these references does not teach all of the limitations of the claimed invention. Accordingly the combination of *Percel* and *Masaki* also does not support a *prima facie* case of obviousness. Applicants therefore respectfully request that the rejection be withdrawn.

For the reasons stated above, Applicants respectfully submit that the claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite the eventual allowance of

[12] *Masaki*, col. 11, line 55 to col. 12, line 42

the claims.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-1283. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. 1.136(a)(3).

Dated: September 24, 2007

Respectfully submitted,
COOLEY GODWARD KRONISH LLP

COOLEY GODWARD KRONISH LLP
CUSTOMER NUMBER 58249
ATTN: Patent Group
777 6th Street, NW, Suite 1100
Washington, DC 20001
Tel: (202) 842-7865
Fax: (202) 842-7899

By: Thomas A. Blink

Thomas A. Blinka
Reg. No. 44,541